

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/03353

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C12N 9/26, 9/24, 9/42; A61K 38/00, 38/43, 38/47, 31/00
US CL :435/183, 200, 195, 201, 209, 325; 424/93.21, 94.1; 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/183, 200, 195, 201, 209, 325; 424/93.21, 94.1; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

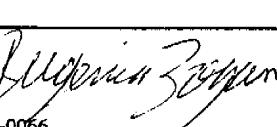
C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------------------|
| X ---- | US 5,362,641 A (FUKS et al) 08 November 1994, see whole document. | 1-8, 13, 22-25, ---- |
| Y ---- | | 9-12, 14-21, 26-53 |
| X ---- | WO 98/46258 A2 (BHASKAR et al) 22 October 1998, see whole document | 1-8, 13, 52-53 ---- |
| Y ---- | | 9-12, 14-51 |
| Y | WANG et al. Basic Fibroblast Growth Factor Enhances Bone-Graft Incorporation: Dose and Time Dependence in Rats. J. Orthop. Res. March 1996. Vol 14. No. 2. pages 316-323, see abstract. | 1-5, 7 and 8, 13 and 22-25, 26-31 |

Further documents are listed in the continuation of Box C.

See patent family annex.

| | | |
|---|-----|--|
| * Special categories of cited documents: | "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| "A" document defining the general state of the art which is not considered to be of particular relevance | "X" | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
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| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | | |
| "O" document referring to an oral disclosure, use, exhibition or other means | "&" | document member of the same patent family |
| "P" document published prior to the international filing date but later than the priority date claimed | | |

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|---|---|
| Date of the actual completion of the international search | Date of mailing of the international search report |
| 16 MAY 2000 | 14 JUN 2000 |
| Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 | Authorized officer RICHARD HUTSON  |
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PCT/US00/03353

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|--------------|--|---------------------------|
| X | Sigma Catalog. 1992. page 275, see Collagenase listing. | 1, 2, 4 and 7 |
| X, P ---- | US 5,968,822 A (PECKER et al) 19 October 1999. see whole document. | 1-14 ---- |
| Y, P | | 15-53 |
| X ---- | WO 91/02977 A1 (FUKS et al) 07 March 1991, see whole document. | 1-8, 13 and 15-21 ---- |
| Y | | 9-12, 14 and 22-53 |